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Methods for Improving Low Magnification Dark-Field Assays

Nanoparticles have comparable sizes to biological molecules and offer the ability to act as biosensors and enhance current therapeutic and diagnostic research, specifically in quantitative assays. However, dark-field microscope-based nanoparticle quantitative assays suffer from a trade-off between sensitivity and usability. Greater assay sensitivity requires intensive manual focus adjustment and positioning, which requires skill and time. Further, high magnification makes it hard to observe all regions of interest, requiring ROI averaging and introducing artificial bias. Using low magnification is also problematic, though, due to the large view area inducing condemnations, dents and scratches, image distortion and lower signal-to-noise ratio.

Researchers at the Biodesign Institute of Arizona State University have developed novel methods for improving low magnification dark-field assays (LMDFA) by overcoming inhomogeneity and low sensitivity issues. A physical pre-treatment step and a signal amplification scheme are employed to improve homogeneous distribution of the biological specimen and enhance the binding affinity and sensitivity during imaging. The result was a tremendous time-saving benefit with an assay duration 14 times shorter on average than non-treated LMDFA and conventional ELISA. These methods can be used in the lab for basic research but could also be used in clinical applications such as diagnostics and treatment monitoring.

These LMDFA enhancements help close the gap and speed up translation of these assays from the laboratory to the clinic for routine analysis applications.

Potential Applications

- Diagnostics

o May be particularly pertinent for quantifying exosomes in serum and cell culture medium

- Treatment monitoring
- Basic research

Benefits and Advantages

- Better homogeneity of nanoparticles
- Low magnification makes imaging easier and avoids artificial bias
- High sensitivity - 6.41 times signal amplification was obtained
- Enhanced binding affinity
- Quantitative identification of biological specimens
- Expedited assays – more than 14 times shorter assay duration could be achieved with the physical pre-treatment step compared to assays without it
- Has a size filtering effect on exomes which could benefit some studies since larger exosomes potentially host more surface markers